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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/032,950	12/27/2001	Tom W. Muir	600-1-231N CON	7862

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EXAMINER	
MITRA, RITA	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 03/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/032,950	MUIR ET AL.	
	Examiner	Art Unit	
	Rita Mitra	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 February 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,17,18 and 25-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,17,18 and 25-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/21/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Applicants' preliminary amendment filed on February 9, 2002, is acknowledged. Amendment to specification has been entered. Claims 1, 2, 17 and 18 have been amended. Claims 3-16, 19-24 have been canceled. New claims 25-39 have been added. Therefore, claims 1, 2, 17, 18 and 25-39 are currently pending and are under examination.

Claim Rejection-35 USC 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17, 18 and dependent claims (25-33) thereto are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 17, 18 and 25-33 are rejected under 35 U.S.C. 112, first paragraph on the ground of lack of enablement, because the skilled artisan, based solely on structural identity of cyclic peptide of claims 17 and 18, would not be able to reconcile whether the protein and/or an analog or variant would be considered for an agent that would be used for a method for treating *S. aureus* infection in a subject. The specification fails to provide any animal model (in vivo).

As for the in vitro use of the peptide, the specification has demonstrated the functional significance of the thiololactone structure in the synthetic AgrDI and AgrDII peptides (Table 1). The peptides were assayed by a Beta-lactamase assay and found to

activate the *agr* response only within their own *S. aureus* class and inhibit the *agr* response only in *S. aureus* strains from the other two classes, however no activation/inhibition activity was detected with linear carboxylate synthetic peptides corresponding to the AgrDI and AgrDII peptides, even at high uM concentrations. The specification asserts from this findings (Example 1, page 16) that the biological activity is restricted to the thiolactone peptides, serves to confirm that this unusual posttranslation modification is present within the secreted AgrD peptides. Further the specification has demonstrated a cyclic thiol ester group is strictly required for the activation/inhibition of the *agr* response (Table 1 and Example 2). Furthermore, the specification has demonstrated in Example 3 that with the linier peptides both the lactone and lactam variants (generated by replacing the thiolactone unit in AgrDII) were unable to activate the *agr* response in any of the three *S. aureus* strains, however, they are able to inhibit the *agr* response in groups I and III *S. aureus* strains (Table 1). The specification interprets from this experiment that the reactive thioester bond is necessary for the activation of the *agr* response in vivo, however it is not necessary for the inhibition. Further it is stated at page 19 that peptide variants which exhibit no activation activity while retaining (or enhancing) inhibitory activity are useful for treating *S. aureus* infections. However, it should be noted that from these findings one cannot extrapolate that these peptides would treat a *S. aureus* infection in a subject. The specification lacks to describe or demonstrate the treatment of *S. aureus* infection in a subject by administration of claimed peptide and their variants.

In summary, the specification describes at page 18 that synthesis of virulence factors and other extracellular proteins responsible for pathogenicity in *Staphylococcus aureus* is under the control of the agr locus. A secreted agr encoded peptide, AgrD is known to be an effector of self-strain activation and cross-strain inhibition of this agr response. The agrD peptides isolated from culture supernatants contain an unusual thiol ester-linked cyclic structure. Further, the chemical synthesis confirms that these agrD peptides contain a thiololactone unit, and that this structure is absolutely necessary for full biological activity in the native peptides. However, this does not suggest that the native peptide with said structure and function would treat a *S. aureus* infection in a

subject. For example, the instant specification does not (pages 11-13) discuss a disease, condition or physiological state which is treated with the protein nor discuss any effect of the said cyclic peptide on the *S. aureus* infection in vivo. The specification describes a propsed model (page 19-20), where an AgrD peptide binds its own AgrC receptor (from the same *S. aureus* class) in a different manner to an AgrC receptor from an another class (Fig 3). However, the proposed model does not suggest or indicate the application of the claimed cyclic peptide towards the treatment of a condition from *S. aureus* infection in a subject. No data is present to demonstrate involvement of the claimed cyclic peptide in any of the disease states due to *S. aureus* infection. Therefore, one skilled artisan would not know how to use the claimed invention without undue experimentation.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1, 2, 17, 18, 25-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 2 and claims dependent thereto (claims 17, 18) are indefinite in regard to the recitation of "synthetic amino acid" and "biosynthetic amino acid." It is unclear that how the two are different.

Claims 1, 2 and claims dependent thereto (claims 17, 18) are drawn to a cyclic peptide capable of inhibiting the *agr* response. The word "capable" is not clear, since it is not clear whether the peptide actually inhibits the *agr* response, or merely have the capability to do so. The word "capable" associates with the latent function only. Amending the claim by deleting the word "capable" would obviate the rejection.

Claims 1, 2, 28 and 29 are rejected under 35 U.S.C. 112, second paragraph, because the abbreviation *"agr"* is not fully spelled out. The term "*agr*" renders the claim

indefinite, it is unclear what "*agr*" is. The full spelled out words should precede an acronym/abbreviation.

Claims 17 and 18 should have the abbreviated terms "*S. aureus*" fully spelled out. The full spelled out words should precede an acronym/abbreviation.

Claims 32 and 33 include extra periods (".."). It is not clear where the claim ends. See MPEP 608.01 (m) (each claim begins with a capital letter and ends with a period). See "Seq. ID No.". Please use "SEQ ID NO:".

Claims 17, 25, 28, 30, 32, 34, 36 are indefinite because they lack essential steps as claimed in the method of treating a *Staphylococcous aureus* infection by administering a peptide of claim 1. The omitted steps are: the site and method of administration, the therapeutically effective amount of the agent and a step whereby the desired outcome and the time for the effective treatment using the said protein can be determined.

Claims 18, 26, 27, 29, 31, 33, 35, 37 are indefinite because they lack essential steps as claimed in the method of treating a *Staphylococcous aureus* infection by administering a peptide of claim 2. The omitted steps are: the site and method of administration, the therapeutically effective amount of the agent and a step whereby the desired outcome and the time for the effective treatment using the said protein can be determined.

Claim Rejections - Nonstatutory Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2 and 38, 39 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2 and 13, 14 of U.S. Patent No. 6,337,385 ('385). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1 and 2 (pending claims) are directed to the broadest scope of the peptide capable of inhibiting the *agr* response. Claims 1 and 2 (pending claims) encompass the cyclic peptide set forth in claim 1 and 2 of patent '385. Claims 38 and 39 are not patentably distinct from claims 13 and 14 of patent '385 because claims 1 and 2 are directed to the broadest scope of the pharmaceutical composition containing the said peptide.

Claim 1 discloses a cyclic peptide comprising a structure wherein X is selected from the group consisting of an amino acid , an amino acid analog, a peptidomimetic and a non-amide isostere, Z is selected from the group consisting of a synthetic amino acid and a biosynthetic amino acid , R is selected from the group consisting of oxygen, nitrogen, sulfur and carbon, n is 0-10 and y is 1-10,

Wherein the cyclic peptide is capable of inhibiting the *agr* response.

This is an obvious variation of claim 1 in the patent '385, which discloses a cyclic peptide with identical structure of the cyclic peptide of claim 1 of current application.

Claim 2 discloses a cyclic peptide comprising the amino acid sequence of NH2-X(n)-Z-X(y)-COOH and a cyclic bond between the Z residue and COOH other than a thioester bond, wherein X is selected from the group consisting of an amino acid , an amino acid analog, a peptidomimetic and a non-amide isostere, Z is selected from the group consisting of a synthetic amino acid and a biosynthetic amino acid , R is selected from the group consisting of oxygen, nitrogen, sulfur and carbon, n is 0-10 and y is 1-10, Wherein the cyclic peptide is capable of inhibiting the *agr* response.

This is an obvious variation of claim 2 in the patent '385, which discloses a cyclic peptide with identical structure of the cyclic peptide of claim 2 of current application.

Claims 38 discloses a pharmaceutical composition comprising a composition of claim 36 containing a protein of claim 17, wherein the carrier is selected from the group consisting of a diluent, an aerosol, a topical carrier, an aqueous solution, a nonaqueous solution, and a solid carrier. This is an obvious variation of claim 13 in the patent '385, which discloses a pharmaceutical composition comprising a composition of claim 11 containing a protein of claim 1, wherein the carrier is selected from the group consisting of a diluent, an aerosol, a topical carrier, an aqueous solution, a nonaqueous solution, and a solid carrier.

Claims 39 discloses a pharmaceutical composition comprising a composition of claim 37 containing a protein of claim 18, wherein the carrier is selected from the group consisting of a diluent, an aerosol, a topical carrier, an aqueous solution, a nonaqueous solution, and a solid carrier. This is an obvious variation of claim 14 in the patent '385, which discloses a pharmaceutical composition comprising a composition of claim 12 containing a protein of claim 2, wherein the carrier is selected from the group consisting of a diluent, an aerosol, a topical carrier, an aqueous solution, a nonaqueous solution, and a solid carrier.

Thus, claims 1, 2, 38 and 39 in present application and claims 1, 2, 13 and 14 in the patent '385 are obvious variations of a cyclic peptide with a structure (as above), wherein the cyclic peptide is capable of inhibiting the *agr* response.

Conclusion

No claims are allowed.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rita Mitra whose telephone number is (703) 605-1211. The Examiner can normally be reached from 9:30 a.m. to 6:30 p.m. on weekdays. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Christopher Low, can be reached at (703) 308-2923. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission.

Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER

Rita Mitra, Ph.D.
February 21, 2003